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37 C.F.R. § 1.8

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June 27, 2005
Date

Steven L. Highlander

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Peter KUFER *et al.*

Serial No.: 09/403,107

Filed: October 14, 1999

For: NOVEL METHOD FOR THE PRODUCTION OF ANTIHUMAN ANTIGEN RECEPTORS AND USES THEREOF

Group Art Unit: 1642

Examiner: D. Blanchard

Atty. Dkt. No.: DEBE:017US/SLH

DECLARATION OF MATHIAS LOCHER UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Mathias Locher, do declare that:

1. My name is Mathias Locher. I am Vice President Preclinical Development at Micromet AG, Munich, Germany. I reside at Odenwaldstrasse 12, 63549 Ronneburg, Germany. I am a citizen of Germany.

2. A fully human IgG1 antibody prepared in accordance with the teachings of the above-captioned application was tested in 20 human prostate carcinoma patients in a Phase I clinical trial with repeated dosing regimen. The patients received two infusions of said antibody with a break of 14 days in between. The first cohort consisting of 2 patients received 10 mg/m^2 body surface area per infusion, whereas the other six cohorts consisting of 3 patients received 20, 40, 64, 102, 164, and 162 mg/m^2 body surface area, respectively.

3. As demonstrated in Appendix 7 (attached hereto), administration of the indicated human anti 17-1A antibody did not elicit an immune response against the human anti 17-1A antibody in any of these patients (no antibodies against the human anti 17-1A antibody could be detected in the serum of these patients on day 28, 35, 42 and 70 after the day of the second infusion). As a positive control, the serum of all patients was spiked with 1μg/ml of an antibody binding to the human anti 17-1A antibody. Appendix 7 exemplifies this control for patient 002004 at day 42 (positive control). Accordingly, none of the 20 patients revealed any detectable antibody titer against the human anti 17-1A antibody clearly underlining the lack of immunogenicity in humans of a human antibody produced according to the method of the present invention.

4. Thus, the present invention provides (two) VH sequences of anti-EpCAM binders derived from the repertoire of unprimed mature human B-lymphocytes, and these molecules are not apparently immunogenic to humans. As required for V-regions derived from the pool

of unprimed mature human B lymphocytes, these sequences show a 100 % identity to the respective human germline sequences.

5. I hereby declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the referenced patent application or any patent issued thereon.

June 1, 2005
Date

Mathias Locher, Ph.D.